BS

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,864	04/27/2001	Martin M. Matzuk	P01925US2 (09807797)	1363

26271 7590 10/29/2004

FULBRIGHT & JAWORSKI, LLP
1301 MCKINNEY
SUITE 5100
HOUSTON, TX 77010-3095

EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 10/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,864	MATZUK ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,24 and 26-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,24 and 26-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/12/2004*. 6/8/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

1. Applicant's amendment filed August 12, 2004 is acknowledged and has been entered. Claim 1 has been amended. Claims 2-7 have been canceled. Claims 1-22 and 25 have been canceled. Claims 23, 24, 26-28 are pending. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejection

3. The claim rejection under 35 USC 101 and 35 USC 112 first paragraph directed to claims 23, 24, 26-28 as lacking utility and enablement is maintained and discussed below. The claim rejection under 35 USC 112 first paragraph directed to claims 23, 24 and 26-28 as lacking adequate written description is maintained and discussed below.

Claim Rejections - 35 USC § 101

4. Once again, claims 23, 24, 26-28 are rejected under 35 U.S.C. 101 because the claimed inventions lack patentable utility due to its not being supported by a specific, substantial, and/or credible utility, or, in the alternative, a well-established utility. The claimed inventions are drawn to an isolated polynucleotide having the polynucleotide sequence set forth in Figure 25 (SEQ ID NO: 16) (claim 23), an isolated polynucleotide that specifically hybridizes with the polynucleotide of claim 23 under hybridization conditions of about 0.3 M NaCl at temperatures of about 50 degrees Celsius to about 55

degrees Celsius, wherein the encoded protein modulates fertility (claim 24) or modulates ovarian development or ovarian function (claim 27) and an isolated nucleic acid that is fully complementary to the polynucleotide sequence of claims 23, 24 or claim 27).

The specification teaches at Figure 25 and in the "Brief Description of the Drawing" at page 13, that SEQ ID NO: 16, which is depicted as Figure 25, is the nucleotide sequence of human O1-236 gene or human NPM2 gene. The specification discloses at page 6 that the O1-236 gene is one of three genes that is ovary-specific and/or oocyte-specific. The specification discloses that these genes and their protein products appear to relate to various cell proliferative or degenerative disorders, especially those involving ovarian tumors, such as germ cell tumors and granulosa cell tumors, or infertility, such as premature ovarian failure. The specification teaches at page 13 that the O1-236 gene expression is highly tissue-specific, being expressed in cells primarily in ovarian tissue. The specification further states that based on the know activity of many other ovary specific proteins, it can be expected that O1-236, as well as fragments and derivatives thereof, will possess biological activities that will make them useful as diagnostic and therapeutic reagents. Nowhere else in the specification is there a teaching of the function of the human O1-236 gene or the encoded protein of said gene. The examples beginning at page 28 through page 46 of the specification discloses the *mouse O1-236 (npm2)* gene (see Figure 5 and SEQ ID NO: 5) and uses of the mouse O1-236 gene in expression analysis with no known function, in cloning procedures, in structural analysis, in chromosomal mapping studies, in subtraction hybridization methods, in knockout mouse protocols, in fertility studies and ovarian-specific expression and *not the human O10236 (npm2) gene.* The specification however fails to provide a specific

asserted utility for the polynucleotides as claimed, the human O1-236 polynucleotide and encoded protein. No direct connection is made between the claimed polynucleotide (human O1-326 (NPM2)) and utility as a modulator of fertility or modulator of ovarian development or ovarian function or association with ovarian tumors. In fact, there is no disclosure anywhere in the specification providing support for a use of the human 01-236 polynucleotide, fragment thereof, or the encoded protein. Merely stating that expression of the O1-236 gene is highly tissue-specific cannot be translated to mean that that sequence is necessarily a marker of ovarian tumors or modulator of fertility or modulator of ovarian development or ovarian function in that tissue. Furthermore, there is no apparent *indicia* of specificity to any disease or ovarian developmental stage. Since the specification sets forth no specific function of the polynucleotide or gene sequence for the claimed SEQ ID NO: 16, or provide any guidance for use of the claimed sequence of SEQ ID NO: 16 or fragments thereof, the claimed encoded protein or its use has no ascribed function as well. Therefore, identifying and/or studying the claimed polynucleotides of the instant invention or fragments thereof or the encoded protein does not define "a real world" context of use because further experimentation would be required to establish a "real world" utility for such sequence that is specific, substantial or credible.

As noted by *Brenner V. Manson*, 383 U.S. 519, 535-536 (1996), "Congress intended that "no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing...a patent is not a hunting license. It is not a reward for the search, but compensation for the successful conclusion". Neither the specification as filed nor any art of record discloses or suggests any property

or activity for the claimed polynucleotide sequences such that another non-asserted utility would be well established for the compounds. Therefore, fore all of the foregoing, the claimed inventions are not supported by either a specific and substantial asserted utility or a well-established utility. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed.

Claim Rejections - 35 USC § 112, first paragraph

5. Claims 23, 24, 26-28 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Moreso, one skilled in the art would not know how to use the claimed invention to modulate fertility or modulate ovarian development and/or ovarian function.

Applicant's Traversal

6. Applicant traverses the rejection on the following grounds: Applicant asserts that the Examiner has failed to meet the requirements of a prima facie showing of no specific and substantial credible utility. Applicant asserts that a specific biological activity has been indicated in the present application (page 6). Applicant also noted that this activity was reasonably correlated to a disease condition. Applicant asserts that the expression of SEQ ID NO: 16 is nearly identical to GDF-9, which when defective in mice, is related to infertility. Applicant states that one with skill in the art would conclude from the specification that a specific and substantial utility is clearly outlined for the claimed invention. Applicant states that furthermore, the examiner states that establishing a utility

for the mouse 01-236 gene fails to establish a utility for the human O10236 gene. Applicants asserts that one with skill in the art would conclude that testing the function of a gene in mice would provide a reasonable correlation for the function of that gene in humans. Applicant argues that a supplemental IDS including NIH report of the history of the mouse as a model system for human disease and animal molecules of ovarian cancer to demonstrate that one skilled in the art considers the mouse model to be an acceptable model as a predictor of disease to humans. Applicant asserts that the Patent Office in this instance appears to be confusing the requirements under the law for obtaining a patent with the requirements for obtaining government approval for marketing drugs. Applicant asserts they do not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating humans where such a utility is asserted. Applicant states that instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the activity and the asserted use. Applicant concludes that the office has not properly established a prima facie case of lack of specific and substantial utility and respectfully request the rejection be withdrawn.

Examiner's Response

7. All of the arguments filed on August 12, 2004 have been thoroughly reviewed and considered but they are not found persuasive for the reasons that follow: In regards to Applicant arguments that a specific biological activity has been indicated in the present invention at page 6, it is noted that a review of page 6 does not establish any specific biological activity for the sequence recited in SEQ ID NO: 16. In fact, there is no

disclosure anywhere on page 6 which specifically suggest a biological activity for the claimed human sequence recited in SEQ ID NO. 16. In regards to Applicant's arguments that the specification notes that SEQ ID NO: 16, is nearly identical to GFD-9, which when defective in mice is related to infertility, it is noted that the Examiner does not find such teachings. There is no teaching anywhere on page 13, which notes that, the expression of SEQ ID NO: 16 is nearly identical to GDF-9. In fact the specification refers to three gene products by name O1-236 and it cannot be determined from the specification at page 6 or 13, whether reference is being made to the mouse O1-236 gene product (SEQ ID NO: 5) or the human O1-236 gene product (SEQ ID NO: 16) or which of the gene products are indeed similar in expression to the GDF-9 gene product. No reference is made at page 13 of the specification to suggest that SEQ ID NO: 16 is indeed the molecule being compared to GDF-9.

In response to Applicant's arguments that testing the function of a gene in mice would provide a reasonable correlation for the function of that gene in human, the Examiner respectfully disagree. While the Examiner acknowledges Applicant's arguments and supplemental IDS establishing that mouse may be used as a model system for human diseases, it is noted that no connection has been made between the claimed sequence (SEQ ID NO: 16) and any diseases. The examiner agrees that studies have been performed on the mouse O1-236 gene sequence, however, the specification provides no evidence whatsoever that would suggest that the sequence of SEQ ID NO: 16 is capable of functioning in the same manner. No connection has been made between the claimed sequence and utility as a modulator of fertility or modulator of ovarian development or ovarian function or association with ovarian tumors. In fact, there is no

disclosure anywhere in the specification providing for a use of the human O1-236 polynucleotide, fragment thereof, or the encoded protein. Further, the specification (page 38) teaches that the human O1-236 gene sequence is about 67% homologous to the sequence of the mouse O1-236 gene. Thus, there is a substantial degree of variably which further substantiates that the different sequence may have different function. At best, the specification appears to speculate that the human sequence (SEQ ID NO: 16) as claimed would indeed have the same function as the mouse sequence (SEQ ID NO: 5) based on some sequence homology. Likewise, Applicant appears to speculate an asserted therapeutic use, without any evidence (biological activity or pharmacological activity) to support such utility. Further experimentation would be required of one skilled in the art to establish a specific, substantial and credible function of the sequence of SEQ ID NO: 16. Applicant's arguments are not sufficient to overcome the rejection under 35 USC 101 and 35 USC 112 first paragraphs. Accordingly, the rejections are maintained.

Claim Rejections - 35 USC § 112: Lack of Adequate Written Description

8. Once again, claims 24, 26-28 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claimed inventions are drawn to an isolated polynucleotide that specifically hybridizes with the polynucleotide of claim 23 under hybridization conditions of about 0.3 M NaCl at temperatures of about 50 degrees Celsius to about 55 degrees Celsius, wherein the encoded protein modulates fertility (claim 24) or that modulates ovarian development or ovarian function (claim 27)

and an isolated polynucleotide that is fully complementary to claim 23 or claim 24 or claim 27 (claims 26 and 28). The specification does not disclose or describe a sequence wherein the encoded protein of SEQ ID NO: 16 modulates fertility or wherein the encoded protein modulates ovarian development or ovarian function. The specification does not disclose or define what is meant by "modulates" in relations to fertility. Nor is thee a limiting definition in the specification to define what is meant by modulation in relations to ovarian development or ovarian function. For example, it cannot be determine if modulates means that the hybridizable nucleic acid molecules increase or enhance or decrease or disrupt ovarian development and/or function or fertility functions. There is no mention anywhere in the specification wherein the function of the claimed polynucleotide is disclosed or defined or a correlation between fertility, ovarian function or ovarian development and the polynucleotides of the instant invention. The examples beginning at page 28, especially examples 10-14, examine fertility and sub-fertility in the *mouse npm2* gene which is depicted as SEQ ID NO: 5 and not the human npm2 gene as recited in SEQ ID NO: 16 of the instant claims. None of the examples examined ovarian development and/or function as it relates to the claimed polynucleotide sequences. The examples merely demonstrated an over-expression of a mouse Npm2 gene in ovarian tissue, which does not equate to a function of modulating ovarian development and ovarian function. The claims as written encompass a large genus of hybridizable nucleic acid molecules or complement sequences not adequately described or disclosed. Each of the claimed inventions is a genus for which a representative number of species for each genus must be disclosed to meet the written description requirement of 112, first paragraph. As set forth in the Court in *Vas Cath Inc. V. Mahurkur*, 19 USPQ2d 1111,

the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date, applicant was in possession of the claimed invention. Absent a written description disclosing a representative number of species of the isolated polynucleotides of claims 24, 26-28, the specification fails to show that applicant was, in fact, "in possession of the claimed invention" at the time of the application for patent was filed.

Applicants' Traversal

9. Applicant traverses the rejection on the following ground(s): Applicant states that well-known case law supports Applicant's position. Applicant states that Applicants asserts that the revised Interim written description guidelines set forth examples of allowable polynucleotide claims defined by functional language, see Example 9, "...a person skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent conditions set forth in the clam yield structurally similar DNAs. Applicant argues that a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention. Applicant assert that the stringent hybridization condition set forth do not encompass an unreasonably large genus, but rather a genus that is strictly defined. Applicant states that additionally, due to the high degree of homology between the mouse and human Npm2 genes, it could be predicted that the species disclosed in the specification as binding to the mouse npm2 gene would also hybridize to the human Npm2 gene. Applicant further notes that during examination the claims must be interpreted as broadly as their terms reasonably allow.

Applicant states that this means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. *In re Zletz,* 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). Applicant submits a supplemental IDS as support that one with skill in the art would understand the term "modulate" without further definition. Applicant request the rejection be withdrawn.

Examiner's Response

10. Applicant's arguments filed on August 12, 2004 have been thoroughly reviewed and considered, but they are not found persuasive for the following reasons: The examiner acknowledges Applicants' arguments, however, it is noted that the specification does not teach, describe or disclose any isolated polynucleotide sequence that hybridizes under any conditions to the sequence of SEQ ID NO: 16. While the specification teaches in the examples, experiments associated with the mouse O1-236 gene or mouse NPM2 gene, no disclosure was found correlating or examining the human Npm2 or O1-236 gene with any ascribed function. Likewise, the specification teaches that the mouse npm2 gene is about 67% homologous to the human Npm2 gene sequence (spec. page 38), but only speculates that the function of the different gene sequences are the same. Thus, it cannot be concluded that any sequence that hybridizes to the mouse npm2 gene would indeed hybridize to human Npm2 gene. Additionally, it cannot be determined that any polynucleotide that hybridizes to the mouse npm2 gene and modulate fertility would in fact hybridize and modulate fertility in the human Npm2. Without some type of guidance and description in the specification, one could not derive at such conclusions. Thus, the Examiner maintains that Applicant has not met the requirements for adequate written description.

In regards to Applicant's arguments concerning the term "modulate", it is noted that the meaning of the term "modulate" is clearly understood by the Examiner, however, the specification does not describe or disclose anywhere, an isolated nucleic acid molecule that modulates (by any interpretation of the term) fertility in human or human cells based on the presence or lack of the human Npm2 gene. There is no disclosure anywhere in the specification demonstrating modulation (by any interpretation of the term) of ovarian development or ovarian function based on the presence or absence of the human Npm2 gene. The Examiner maintains that the specification only demonstrates over-expression in ovarian tissue, which clearly cannot be translated as a function in that tissue. Thus contrary to Applicant's arguments, the specification does not provide adequate written description for the claims 24, 26-28 as required under 35 USC 112 first paragraph. Accordingly, the specification fails to show that Applicant was, in fact, "in possession of the claimed invention" at the time the application for patent was filed.

Conclusion

11. No claims are allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory

action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
10/25/04